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Stress hyperglycemia ratio: an independent predictor for in-hospital major adverse cardiovascular and cerebrovascular events in patients with ST-segment elevation myocardial infarction

Wen Guo¹, Jijia Zhu¹ and Wenxian Liu^{1*}

Abstract

Background To assess the predictive accuracy of the stress hyperglycemia ratio (SHR) for in-hospital major adverse cardiovascular and cerebrovascular events (MACCE) in patients with ST-segment elevation myocardial infarction (STEMI).

Methods A total of 1,944 patients were enrolled within 24 h of a new STEMI diagnosis. The SHR was obtained by dividing the blood glucose level at admission by the estimated average glucose. MACCE were defined as acute cerebral infarction, mechanical complications of myocardial infarction, cardiogenic shock, and all-cause death. Patients were then categorized into the MACCE and non-MACCE groups according to the occurrence of in-hospital MACCE. Propensity score matching was used to balance confounding factors, and logistic regression was used to identify the potential predictive factors for MACCE.

Results A total of 276 patients were included after 1:1 matching, and the confounding factors were balanced between the two groups. The SHR was an independent predictor of in-hospital MACCE (odds ratio = 10.06, 95% confidence interval: 4.16–27.64, $P < 0.001$), while blood glucose at admission was not. The SHR was also an independent predictor for in-hospital MACCE in nondiabetic patients with STEMI (odds ratio = 11.26, 95% confidence interval: 3.05–55.21, $P < 0.001$).

Conclusion SHR is an independent predictor of in-hospital MACCE in patients with acute STEMI, especially in nondiabetic patients.

Keywords Diabetes mellitus, MACCE, Stress hyperglycemia ratio, ST-segment elevation myocardial infarction

Background

ST-segment elevation myocardial infarction (STEMI) is the most severe type of coronary heart disease. With advances in primary prevention, interventional therapy, and drug therapy, the incidence of STEMI has declined in developed countries. However, it remains a leading cause of death worldwide [1]. A previous study reported that diabetes mellitus (DM), one of the well-recognized

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risk factors for coronary heart disease, increases the morbidity and mortality rates of patients with acute myocardial infarction (AMI) [2]. Subsequent studies identified stress hyperglycemia as a predictor of prognosis for AMI patients [3, 4]. In 2015, Roberts et al. proposed replacing conventional blood glucose levels with the stress hyperglycemia ratio (SHR) to predict the severity of critical illness [5]. Another study reported that the SHR is closely associated with the short-term prognosis of AMI patients [6]. However, it remains unclear whether the SHR, as a monitoring parameter, can be used as an independent predictor in patients with STEMI.

In the present study, we aimed to evaluate the predictive value of the SHR for in-hospital major adverse cardiovascular and cerebrovascular events (MACCE) in patients with newly diagnosed STEMI within the previous 24 h. As the high predictive value of stress hyperglycemia for the prognosis of AMI may be related to its effects on myocardial metabolism and insulin treatment for DM [7, 8], we also evaluated the predictive potential of the SHR in STEMI patients without diabetes (nondiabetic subgroup).

Methods

Study participants

In this retrospective study, 2,616 patients who were diagnosed with STEMI in our hospital from January 1st, 2015, to December 31st, 2019, were consecutively screened. The inclusion criteria were as follows: (1) met the diagnostic criteria for STEMI [9] and (2) aged over 18 years.

Patients were excluded if: (1) STEMI was diagnosed more than 24 h previously or (2) blood glucose levels at admission (Glu) or glycated hemoglobin (HbA1c) levels were not measured within 24 h of admission. Finally, 1,944 patients were recruited. The process of recruitment is shown in Fig. 1. This study was approved by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University (Approval number: 2022170X). All patients provided written informed consent.

Because only 7.1% of the enrolled patients had poor outcomes, 1:1 nearest neighbor propensity score matching (PSM) was used to control possibly biased baseline covariates. The propensity score was estimated using a multivariate logistic regression model. As gender, age, and history of hypertension, diabetes, chronic kidney disease, and smoking, as well as coronary vascular conditions are independent risk factors for poor prognosis of STEMI [1], the demographic characteristics, medical history, and coronary vascular conditions of patients were included in the PSM model for 1:1 matching.

Definitions

STEMI was diagnosed if there was a fall and/or rise in the cardiac troponin (cTn) level, with at least one value above the 99th percentile upper reference limit and at least one of the following symptoms: development of pathological Q waves, new ST-segment elevation on electrocardiogram, myocardial ischemia-related symptoms, and imaging evidence of new regional wall motion abnormality or

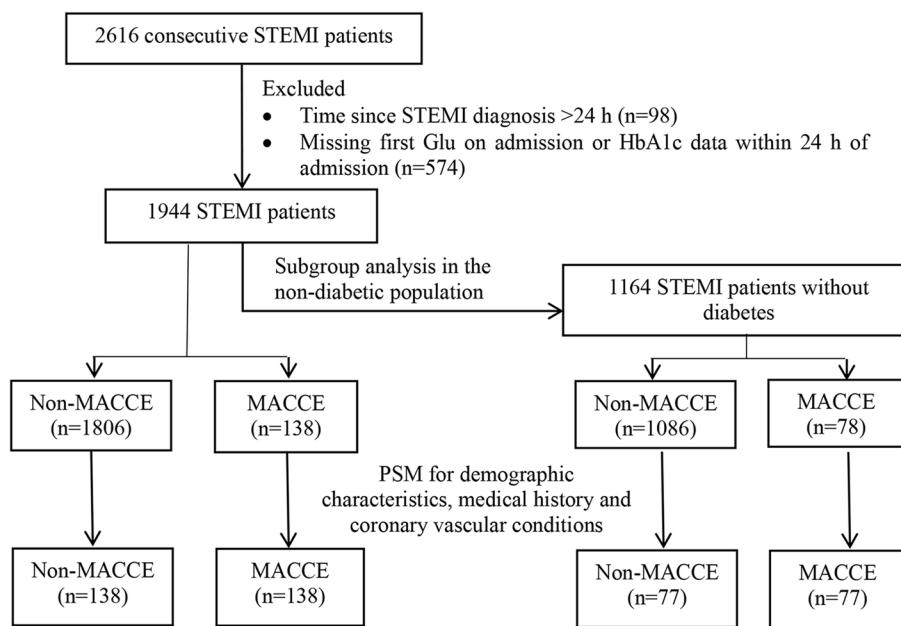


Fig. 1 Flowchart of patient enrollment and subgroup analysis

new loss of viable myocardium in a pattern consistent with ischemic etiology [9].

The SHR was defined as the Glu divided by the estimated average glucose derived from HbA1c [5]. The following formula was used: $SHR = \text{Glu (within 24 h of STEMI onset)} / [(1.59 \times \text{HbA1c}) - 2.59]$.

The main observational outcome was in-hospital MACCE, defined as acute ischemic stroke, mechanical complications of myocardial infarction (MI), cardiogenic shock, and all-cause death.

Patients with no previously diagnosed DM or a HbA1c level of less than 6.5% were considered nondiabetic [10].

Data collection

The demographic characteristics and data regarding the history of smoking, hypertension, dyslipidemia, chronic renal disease, stroke, and coronary revascularization of all patients were collected from medical records based on standardized definitions by two experienced data inspectors. The number of significantly narrowed vessels was counted as any coronary arteries with $\geq 50\%$ stenosis in the three main branches without considering left main artery disease. The following clinical data were also collected: diastolic blood pressure (DBP) and systolic blood pressure (SBP) at admission, respiratory rate, heart rate (HR), Killip class, occurrence of arrhythmia (new atrial or ventricular arrhythmias after STEMI), usage of intra-aortic balloon pump (IABP), ventilator, blood platelet count, white blood cell (WBC) count, and levels of hemoglobin, alanine transaminase, albumin, aspartate aminotransferase, C-reactive protein (CRP), serum creatinine (Cr), Glu, HbA1c, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, total triglycerides, total cholesterol, brain natriuretic peptide (BNP), creatine kinase, lactate dehydrogenase, cardiac troponin I, and serum potassium. All blood samples were analyzed immediately after collection in our medical center. The left ventricular ejection fraction (LVEF) and left ventricular end-diastolic dimension were measured by echocardiography using Simpson's method.

Statistical analysis

Continuous variables are expressed as mean \pm standard deviation or median (25th percentile, 75th percentile) according to the results of the normality test. Differences in continuous data between two groups were assessed by independent sample *t*-test or Mann–Whitney U test. Categorical data are shown as number (percentage). Differences in categorical variables between two groups were analyzed by χ^2 or Fisher's exact test.

Patients in the MACCE group were matched to those in the non-MACCE group using a structured, iterative propensity score model, with the primary objective

of maximizing the balance in the distribution of possible confounders between the two groups. Then, PSM was performed separately for all patients and the non-diabetic subgroup, which included all baseline data, such as age, gender, medical history, and coronary vascular conditions. The corresponding propensity score of the variables was calculated for each patient in the MACCE group. A nearest neighbor matching algorithm was used to match patients in the MACCE group with those in the non-MACCE group at a 1:1 ratio (with no replacement) within $0.2 \times$ standard deviation of the logit of the propensity score. To determine whether PSM achieved balance in all potential confounders, all baseline characteristics after PSM were compared between the groups.

To screen independent risk factors for patient prognosis, indicators with statistical significance after PSM were included in the multivariate logistic regression analysis using forward selection. $P < 0.05$ was considered statistically significant. R version 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria) was used to conduct all statistical analyses and to prepare all graphical presentations.

Results

Baseline data

A total of 1,944 patients who were diagnosed with STEMI were enrolled. The baseline characteristics of these patients are presented in Table 1. The mean age of this cohort was 58.43 years. Among them, 1505 (77.4%) were male and 1,689 (86.9%) underwent percutaneous coronary intervention (PCI). During hospitalization, 138 (7.1%) patients experienced MACCE, including 28 (1.4%) deaths. The SHR of patients who experienced MACCE was higher than that of those who did not experience MACCE ($P < 0.05$).

The gender and history of smoking, hypertension, dyslipidemia, stroke, peripheral arterial disease, coronary artery bypass grafting, and PCI were comparable between the MACCE and non-MACCE groups. Patients in the MACCE group were older and had a higher rate of chronic kidney disease than those in the non-MACCE group. The rate of primary PCI and the incidence rates for disease involving the right coronary artery, left circumflex coronary artery, left anterior descending coronary artery, and multiple vessels were comparable between the two groups. The incidence of left main coronary artery disease was higher in the MACCE group than in the non-MACCE group. Meanwhile, patients who experienced MACCE also showed a higher HR, respiratory rate, Killip class, occurrence of arrhythmia, and usage of IABP and ventilator, but lower blood pressure (both SBP and DBP), albumin level, total triglyceride level, and LVEF than those who did not experience MACCE.

Table 1 Demographic characteristics, medical history, and coronary vascular conditions of all patients before and after propensity score matching (PSM)

Variables	Before PSM				After PSM			
	Non-MACCE (n = 1806)	MACCE (n = 138)	t/χ ²	P-value	Non-MACCE (n = 138)	MACCE (n = 138)	t/χ ²	P-value
Age	58.21 ± 11.83	61.36 ± 2.14	2.971	0.003*	61.36 ± 13.96	61.36 ± 12.14	0.005	0.996
Gender (male)	1403 (77.7%)	102 (73.9%)	1964.760	0.36	105 (76.1%)	102 (73.9%)	256.569	0.781
Medical history								
Hypertension	992 (54.9%)	83 (60.1%)	1980.397	0.272	72 (52.2%)	83 (60.1%)	292.407	0.225
Smoking	1131 (62.6%)	86 (62.3%)	1793.182	> 0.99	86 (62.3%)	86 (62.3%)	221.719	> 0.99
Dyslipidemia	231 (12.8%)	25 (18.1%)	2024.040	0.098	27 (19.6%)	25 (18.1%)	247.947	0.878
CKD	145 (8.0%)	31 (22.46%)	2148.302	< 0.001*	30 (21.7%)	31 (22.5%)	219.631	> 0.99
Prior Stroke	157 (8.7%)	18 (13.0%)	2017.455	0.117	16 (11.6%)	18 (13.0%)	250.294	0.855
Prior PAD	26 (1.4%)	2 (1.4%)	1768.430	< 0.99	1 (0.7%)	2 (1.4%)	215.928	> 0.99
Prior PCI	192 (10.6%)	13 (9.4%)	1898.249	0.762	12 (8.7%)	13 (9.4%)	199.563	> 0.99
Prior CABG	12 (0.7%)	2 (1.4%)	1927.067	0.597	2 (1.4%)	2 (1.4%)	209.719	> 0.99
Coronary vascular condition								
Primary PCI	1576 (87.3%)	113 (81.9%)	2025.545	0.094	109 (79.0%)	113 (81.9%)	265.470	0.649
LM	120 (6.6%)	20 (14.5%)	2148.579	0.001*	19 (13.8%)	20 (14.5%)	218.623	> 0.99
LAD	1284 (71.1%)	100 (72.5%)	1888.804	0.807	96 (69.6%)	100 (72.5%)	262.820	0.691
LCX	810 (44.9%)	67 (48.6%)	1950.018	0.451	65 (47.1%)	67 (48.6%)	244.903	0.904
RCA	918 (50.8%)	72 (52.2%)	1883.711	0.829	74 (53.6%)	72 (52.2%)	244.903	0.904
Multi-vessels	1564 (86.6%)	113 (81.9%)	2006.296	0.155	74 (53.6%)	113 (81.9%)	265.470	0.649

PSM Propensity score matching, MACCE Major adverse cardiovascular and cerebrovascular events, CKD Chronic kidney disease, PAD Peripheral arterial disease, PCI Percutaneous coronary intervention, CABG Coronary artery bypass grafting, LM left main coronary artery, LAD Left anterior descending coronary artery, LCX Left circumflex coronary artery, RCA Right coronary artery

* P < 0.05

PSM was then performed to eliminate confounding factors. STEMI patients in the MACCE and non-MACCE groups (n = 138 per group), with no significant difference in demographic characteristics, medical history, or coronary vascular conditions, were further analyzed. After matching, the SHR of the MACCE group was higher than that of the non-MACCE group (1.00 ± 0.30 vs. 1.18 ± 0.43, P < 0.001). Moreover, patients in the MACCE group showed a significantly higher HR, Killip class, occurrence of arrhythmia, usage of IABP and ventilator, WBC, Glu, CRP, and Cr, but lower SBP, DBP, HbG, and LVEF than those in the non-MACCE group (P < 0.05) (Fig. 2, Tables 1–2).

Predictive value of SHR for in-hospital outcomes in patients with STEMI

The 138 cases with MACCE included 28 cases of all-cause death, 5 cases of acute ischemic stroke, 21 cases with mechanical complications of MI, and 95 cases of cardiogenic shock. After PMS matching, three factors related to in-hospital MACCE were included in the multivariate logistic regression analysis: SHR (odds ratio [OR] = 10.06, 95% confidence interval [CI]: 4.16–27.64, P < 0.001), occurrence of arrhythmia (OR = 2.87, 95% CI:

1.10–8.47, P = 0.040), and acute heart failure (OR = 4.93, 95% CI: 2.31–11.20, P < 0.001). They all were independent risk factors for in-hospital MACCE. SBP was a protective factor for in-hospital MACCE in patients with STEMI (OR = 0.98, 95% CI: 0.97–0.99, P = 0.002), whereas Glu was not an independent risk factor for MACCE (Table 3, Fig. 3).

Predictive value of SHR in nondiabetic patients

To eliminate the effects of long-term hyperglycemia on the metabolism of patients with DM and the effects of regular use of insulin and other hypoglycemic drugs on the prognosis, subgroup analysis was performed in people without DM. Before PSM, the non-MACCE and MACCE groups included 1,086 and 78 nondiabetic patients, respectively. After PSM, the non-MACCE and MACCE groups included 77 nondiabetic patients each. No significant difference in baseline characteristics, including age, gender, medical history, and coronary vascular conditions, was found between the two groups. The SHR remained higher in the MACCE group than in the non-MACCE group (0.99 ± 0.23 vs 1.24 ± 0.45, P < 0.001). The HR, occurrence with Killip III&IV and arrhythmia, usage of IABP and ventilator, WBC, Glu, CRP, and Cr in

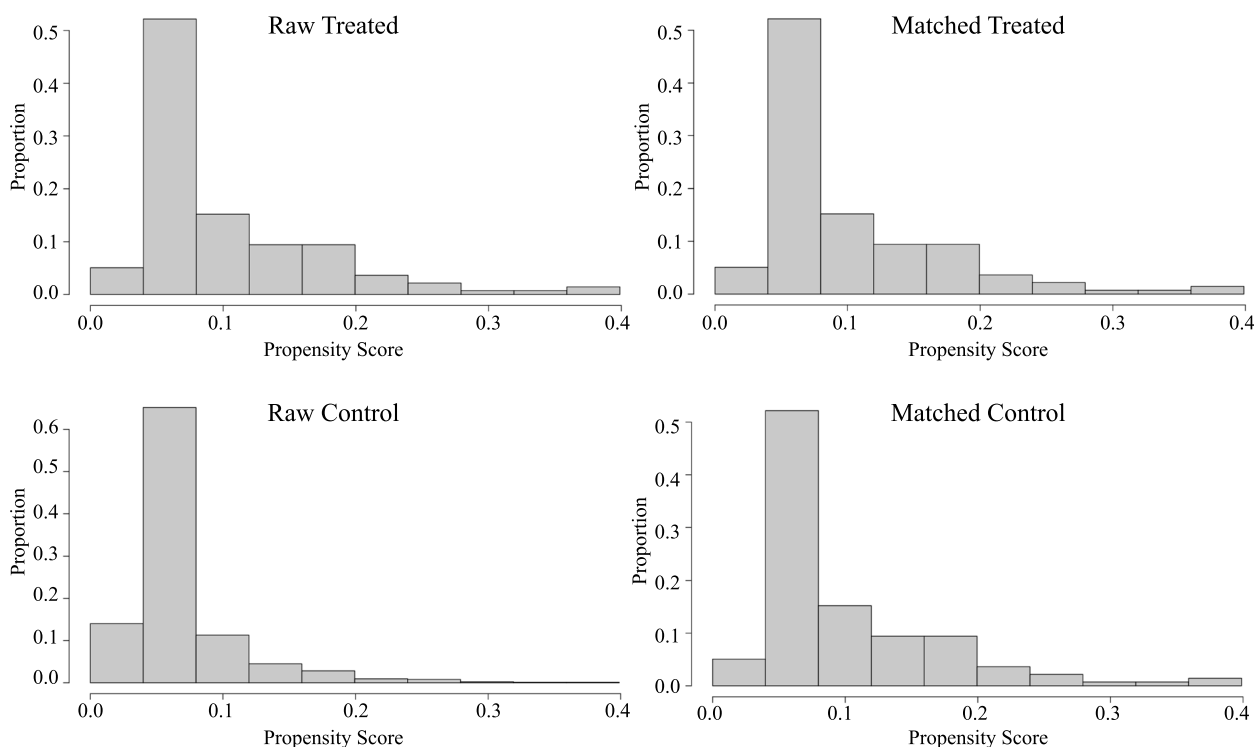


Fig. 2 Clinical features of STEMI patients before and after propensity score matching

the MACCE group were significantly higher, while the SBP, DBP, HBG, TC, and LVEF were significantly lower than those in the non-MACCE group ($P < 0.05$) (Table 4, Fig. 4).

Among nondiabetic patients, 78 cases experienced MACCE, including 14 cases of all-cause death, 2 cases of acute ischemic stroke, 11 cases with mechanical complications of MI, and 57 cases of cardiogenic shock. After PMS matching, 77 cases of MACCE were included, including 13 cases of all-cause death, 2 cases of acute ischemic stroke, 10 cases with mechanical complications of MI, and 57 cases of cardiogenic shock. Four factors related to in-hospital MACCE in patients with STEMI were included in the multivariate logistic regression analysis, including the SHR (OR = 11.26, 95% CI: 3.05–55.21, $P < 0.001$), occurrence of arrhythmia (OR = 16.79, 95% CI: 2.72–328.46, $P = 0.011$), acute heart failure (OR = 14.35, 95% CI: 3.47–98.88, $P = 0.001$), and CRP (OR = 1.05, 95% CI: 1.02–1.09, $P = 0.003$). All four factors were found to be independent risk factors for in-hospital MACCE in the nondiabetic subgroup. However, Glu was not an independent risk factor for in-hospital MACCE in this subgroup (Table 5, Fig. 5).

Discussion

In this study, STEMI patients were recruited independent of the occurrence of MACCE, and age, cardiac function, renal function, and coronary vascular conditions were included in a PSM model. Our findings suggest that the SHR is an independent predictor for in-hospital MACCE in this population.

Assessment of the prognostic value of several inexpensive and readily available laboratory variables, such as serum glucose level, in STEMI is important. In 2009, Horne et al. from the Intermountain Medical Center developed the Intermountain Risk Score (IMRS) to evaluate the overall health status and estimate the mortality risk from all causes in the general population [11]. Several studies have shown that the IMRS can predict mortality in patients with STEMI or STEMI accompanied by cardiogenic shock [12, 13].

Furthermore, stress hyperglycemia is associated with adverse outcomes in AMI [14]. Previous studies have shown that the blood glucose level is an independent risk factor for in-hospital death in patients with cardiogenic shock [15, 16]. A positive correlation between stress hyperglycemia and intracoronary thrombotic burden has been reported [17]. Khalfallah et al. found that stress

Table 2 Clinical characteristics and biochemical variables of all STEMI patients before and after PSM

Variables	Before PSM			After PSM		
	Non-MACCE (n = 1806)	MACCE (n = 138)	P-value	Non-MACCE (n = 138)	MACCE (n = 138)	P-value
Clinical characteristics						
SBP (mmHg)	120.27 ± 20.53	103.77 ± 26.64	3.456	121.86 ± 22.91	103.77 (26.64)	3.360
DBP (mmHg)	73.54 ± 12.87	64.88 ± 16.32	3.365	72.86 ± 12.67	64.88 ± 16.32	3.477
HR (bpm)	76.82 ± 15.31	88.42 ± 22.69	3.307	79.54 ± 17.50	88.42 ± 22.69	3.394
RR (bpm)	18.54 ± 3.04	19.57 ± 3.78	3.328	18.88 ± 3.09	19.57 ± 3.78	1.655
Killip III&IV	63 (3.5%)	52 (37.7%)	2154.697	11 (8.0%)	52 (37.7%)	359.095
Arrhythmia	65 (3.6%)	28 (20.3%)	2149.143	6 (4.3%)	28 (20.3%)	353.539
IABP	253 (14.0%)	83 (60.1%)	2141.750	24 (17.4%)	83 (60.1%)	353.625
Ventilator	32 (1.8%)	34 (24.6%)	2149.143	7 (5.1%)	34 (24.6%)	353.711
Biochemical variables						
WBC (× 10 ⁹ /L)	9.63 ± 3.39	11.95 ± 4.59	3.498	9.96 ± 3.90	11.95 ± 4.59	3.377
HGB (g/L)	136.95 ± 17.19	138.46 ± 18.91	0.991	132.02 ± 19.47	138.46 ± 18.91	2.769
PLT (× 10 ⁹ /L)	208.65 ± 60.17	208.08 ± 57.03	0.108	201.89 ± 51.95	208.08 ± 57.03	0.942
ALT (U/L)	53.75 ± 127.33	143.15 ± 517.96	3.446	59.39 ± 147.29	143.15 ± 517.96	1.819
ALB (g/L)	38.90 ± 4.17	37.60 ± 4.72	3.296	37.61 ± 4.58	37.97 ± 5.66	0.575
AST (U/L)	141.88 ± 227.76	240.94 ± 522.43	3.365	144.69 ± 283.99	240.94 ± 522.43	1.896
Cr (μmol/L)	85.06 ± 40.97	101.55 ± 60.88	3.985	103.84 ± 49.17	101.55 ± 60.88	0.343
Glucose (mmol/L)	7.70 ± 3.03	9.03 ± 3.44	3.328	7.21 ± 2.91	9.03 ± 3.44	3.370
HbA1c (%)	6.54 ± 1.52	6.58 ± 1.50	0.331	6.61 ± 1.50	6.58 ± 1.50	0.170
SHR	1.00 ± 0.30	1.18 ± 0.43	3.399	0.92 ± 0.28	1.18 ± 0.43	3.394
TG (mmol/L)	1.75 ± 1.13	1.45 ± 1.15	2.971	1.62 ± 0.95	1.45 ± 1.15	1.296
TC (mmol/L)	4.50 ± 1.04	4.33 ± 1.20	1.752	4.36 ± 1.02	4.33 ± 1.20	0.192
HDL-C (mmol/L)	1.01 ± 0.28	1.03 ± 0.30	0.754	0.97 ± 0.26	1.03 ± 0.30	1.586
LDL-C (mmol/L)	2.83 ± 0.86	2.70 ± 0.95	1.707	2.76 ± 0.82	2.70 ± 0.95	0.553
CRP (mg/L)	11.87 ± 11.54	17.72 ± 13.77	3.498	13.73 ± 12.23	17.72 ± 13.77	2.401
BNP (ng/L)	760.38 ± 1584.71	1051.89 ± 2181.27	1.101	883.94 ± 1342.41	1051.89 ± 2181.27	0.505
cTnI (ng/ml)	36.97 ± 82.01	45.75 ± 93.43	1.193	38.06 ± 72.39	45.75 ± 93.43	0.758
CK (U/L)	1097.85 ± 1518.40	1581.33 ± 2547.54	3.296	980.20 ± 1417.10	1581.33 ± 2547.54	2.424
LDH (U/L)	448.59 ± 404.61	537.39 ± 563.50	2.411	456.44 ± 538.40	537.39 ± 563.50	1.221
K (mmol/L)	4.06 ± 0.46	4.08 ± 0.52	0.711	4.06 ± 0.43	4.08 ± 0.52	0.417
LVEDD (mm)	49.78 ± 5.88	50.34 ± 7.68	1.011	50.30 ± 5.70	50.34 ± 7.68	0.051
LVEF (%)	54.45 ± 12.9	47.98 ± 11.29	3.403	52.27 ± 11.71	47.98 ± 11.29	2.994

PSM Propensity score matching, MACCE Major adverse cardiovascular and cerebrovascular events, SBP Systolic blood pressure, DBP Diastolic blood pressure, HR Heart rate, RR Respiratory rate, IABP Intra-aortic balloon pump, WBC White blood cell, HGB Hemoglobin, PLT Blood platelet count, ALT Alanine transaminase, ALB Albumin, AST Aspartate aminotransferase, Cr Serum creatinine, Glu first blood glucose on admission within 24 h, HbA1c Glycosylated hemoglobin, SHR Stress hyperglycemia ratio, TG Total triglycerides, TC Total cholesterol, HDL-C High-density lipoprotein cholesterol, LDL-C Low-density lipoprotein cholesterol, CRP C-reactive protein, BNP Brain natriuretic peptide, cTnI Cardiac troponin I, CK Creatine kinase, LDH Lactate dehydrogenase, LVEDD Left ventricular end-diastolic dimension, LVEF Left ventricular ejection fraction

* P < 0.05

Table 3 Multivariate logistic regression analysis of predictors of in-hospital outcomes in STEMI patients after PSM

Variables	β	S.E	OR	95% CI	P-value
Arrhythmia	1.05	0.51	2.87	1.10–8.47	0.040*
Killip III&IV	1.60	0.40	4.93	2.31–11.20	<0.001*
SBP	-0.02	0.96	0.98	0.97–0.99	0.002*
SHR	2.31	0.48	10.06	4.16–27.64	<0.001*

S.E. Standard error, OR Odds ratio, CI Confidence interval, SBP Systolic blood pressure, SHR Stress hyperglycemia ratio

* P < 0.05

hyperglycemia is associated with increased incidences of cardiogenic shock, contrast-induced nephropathy, and no-reflow phenomenon, as well as higher mortality, in nondiabetic STEMI patients undergoing primary PCI [6]. Furthermore, hyperglycemia during perioperative coronary revascularization leads to increased inflammatory platelet activity and endothelial dysfunction, which may be related to plaque instability [18]. A positive correlation between hyperglycemia at admission and MI size has also been observed in patients with STEMI [19, 20]. The above data suggest that stress hyperglycemia may indicate the severity of acute disease and be predictive of prognosis.

Patients with STEMI are under stress conditions, which induce the secretion of a large amount of cortisol hormones, such as epinephrine and catecholamines, from the adrenal cortex, resulting in a sharp rise in blood glucose in a short period of time. Previous evidence demonstrated that stress hyperglycemia promotes the production of free fatty acids, which aggravates oxidative stress, endothelial damage, and inflammation, and

increases cortisol hormone and blood glucose levels [21]. Endothelial dysfunction, microcirculation impairment, thrombosis, and stress hyperglycemia all contribute to the poor prognosis of patients with STEMI [22, 23]. Thus, stress hyperglycemia may contribute to worse short-term outcomes in patients with higher glucose levels but without previously diagnosed DM.

Stress hyperglycemia has been identified as a potential predictor for adverse cardiovascular events in patients with coronary heart disease. The study by Mone et al. [24] showed that the risk of re-hospitalization with chest pain is significantly increased in patients with ischemia and nonobstructive coronary arteries who have a SHR > 1 for 1 year, suggesting that the SHR may be used as an independent risk factor for these patients. Additionally, the SHR has been identified as a potential predictor for death in patients with MI, especially in those without DM [7]. The possible reasons are as follows: (1) chronic hyperglycemia may protect the myocardium via hypoxia-induced apoptosis and necrosis [25]; (2) the prognosis of DM patients with MI is poor. In addition to hyperglycemia, the influence of diabetic cardiomyopathy should also be excluded [26]; and (3) diabetic patients are more often treated with insulin and other hypoglycemic drugs. Previous studies have confirmed that insulin can reduce the mortality of patients with AMI [27]. Nondiabetic patients with STEMI tend to have a worse prognosis than those with DM. The HORIZONS-AMI trial, a prospective study of 3,405 STEMI patients undergoing direct PCI, reported a positive correlation between acute hyperglycemia and mortality in the nondiabetic subgroup, which was stronger than that in the DM subgroup [28]. These data imply that the effect of acute hyperglycemia

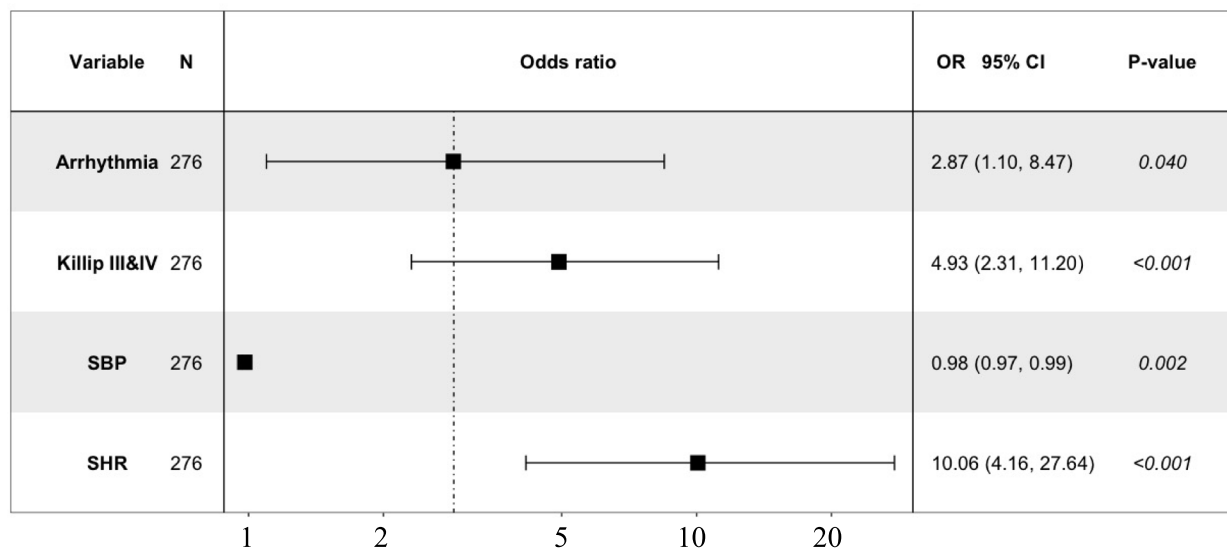


Fig. 3 Multivariate logistic regression analysis of predictors of in-hospital outcomes among all STEMI patients after PSM

Table 4 Characteristics of STEMI patients without diabetes before and after PSM

Variables	Before PSM				After PSM			
	Non-MACCE (n = 1086)	MACCE (n = 78)	t/χ ²	P-value	Non-MACCE (n = 77)	MACCE (n = 77)	t/χ ²	P-value
Age	57.04 ± 11.96	59.95 ± 12.70	2.066	0.039*	60.48 ± 13.80	59.78 ± 12.69	0.328	0.743
Gender (male)	878 (80.8%)	60 (76.9%)	1944.678	0.485	53 (68.8%)	60 (77.9%)	163.058	0.274
Medical history								
Hypertension	560 (51.6%)	38 (48.7%)	1907.687	0.712	34 (44.2%)	38 (49.4%)	146.707	0.628
Smoking	716 (65.9%)	48 (61.5%)	1941.396	0.506	43 (55.8%)	48 (62.3%)	151.810	0.512
Dyslipidemia	128 (11.8%)	12 (15.4%)	1950.966	0.445	11 (14.3%)	12 (15.6%)	107.477	> 0.99
CKD	74 (6.8%)	11 (14.1%)	2053.498	0.04*	7 (9.1%)	10 (13.0%)	147.645	0.607
Prior Stroke	81 (7.5%)	6 (7.7%)	1768.430	> 0.99	6 (7.8%)	6 (7.8%)	110.623	> 0.99
Prior PAD	11 (1.0%)	2 (2.6%)	1944.991	0.483	2 (2.6%)	1 (1.3%)	113.385	> 0.99
Prior PCI	89 (8.2%)	4 (5.1%)	1949.545	0.454	4 (5.2%)	4 (5.2%)	107.477	> 0.99
Coronary vascular condition								
Primary PCI	966 (89.0%)	67 (85.9%)	1938.740	0.523	66 (85.7%)	67 (87.0%)	111.698	> 0.99
LM	67 (6.2%)	10 (12.8%)	2052.755	0.041*	8 (10.4%)	10 (13.0%)	138.000	0.802
LAD	768 (70.7%)	57 (73.1%)	1899.822	0.754	52 (67.5%)	57 (74.0%)	153.299	0.478
LCX	768 (70.7%)	57 (73.1%)	1899.822	0.754	46 (59.7%)	40 (51.9%)	156.020	0.417
RCA	542 (49.9%)	36 (46.2%)	1926.426	0.601	38 (49.4%)	36 (46.8%)	133.365	0.872
Multi-vessels	958 (88.2%)	67 (85.9%)	1915.385	0.668	66 (85.7%)	67 (87.0%)	112.602	> 0.99
Clinical characteristics								
SBP (mmHg)	119.74 ± 19.81	103.13 ± 25.49	3.395	< 0.001*	121.44 ± 21.83	103.17 ± 25.65	3.620	< 0.001*
DBP (mmHg)	73.88 ± 12.93	65.00 ± 14.95	3.325	< 0.001*	73.86 ± 13.73	65.06 ± 15.04	3.386	< 0.001*
HR (bpm)	75.76 ± 14.55	90.72 ± 25.16	3.622	< 0.001*	76.39 ± 15.16	90.62 ± 25.31	3.620	< 0.001*
RR (bpm)	18.37 ± 2.85	19.56 ± 4.20	3.296	0.001*	18.78 ± 3.19	19.51 ± 4.19	1.210	0.228
Killip III&IV	28 (2.6%)	27 (34.6%)	2148.302	< 0.001*	2 (2.6%)	27 (35.1%)	215.075	< 0.001*
Arrhythmia	33 (3.0%)	19 (24.4%)	2158.858	< 0.001*	1 (1.3%)	19 (24.7%)	214.228	< 0.001*
IABP	124 (11.4%)	43 (55.1%)	2151.251	< 0.001*	13 (16.9%)	43 (55.8%)	217.180	< 0.001*
Ventilator	10 (0.9%)	16 (20.5%)	2164.131	< 0.001*	2 (2.6%)	16 (20.8%)	212.797	0.001*
Biochemical variables								
WBC (× 10 ⁹ /L)	9.50 ± 3.22	12.61 ± 4.68	3.487	< 0.001*	9.48 ± 3.60	12.59 ± 4.70	3.505	< 0.001*
HGB (g/L)	138.13 ± 16.35	139.30 ± 19.30	0.604	0.546	133.23 ± 17.62	139.46 ± 19.37	2.093	0.038*
PLT (× 10 ⁹ /L)	209.29 ± 60.05	204.74 ± 51.87	0.653	0.514	207.98 ± 50.27	206.58 ± 49.58	0.174	0.862
ALT (U/L)	52.01 ± 84.69	78.31 ± 192.27	2.328	0.02*	49.51 ± 47.79	56.97 ± 43.97	0.994	0.322
ALB (g/L)	39.12 ± 4.02	37.75 ± 4.80%	2.882	0.004*	38.88 ± 4.46	37.91 ± 5.30	1.195	0.234
AST (U/L)	138.19 ± 183.38	209.12 ± 385.82	2.971	0.003*	155.63 ± 170.20	173.26 ± 221.85	0.552	0.582
Cr (μmol/L)	82.66 ± 34.85	97.28 ± 62.62	3.296	0.001	91.18 ± 74.45	95.57 ± 61.17	0.400	0.69
Glu (mmol/L)	6.45 ± 1.66	8.00 ± 2.90	3.358	< 0.001*	6.39 ± 1.47	7.99 ± 2.92	3.421	< 0.001*
HbA1c (%)	5.67 ± 0.38	5.71 ± 0.35	1.018	0.309	5.73 ± 0.41	5.71 ± 0.34	0.424	0.672
SHR	1.01 ± 0.27	1.24 ± 0.45	3.622	< 0.001*	0.99 ± 0.23	1.24 ± 0.45	3.460	< 0.001*
TG (mmol/L)	1.67 ± 0.97	1.30 ± 0.61	3.296	0.001	1.69 ± 1.08	1.30 ± 0.61	2.646	0.009*
TC (mmol/L)	4.51 ± 1.03	4.36 ± 1.13	1.216	0.224	4.44 ± 1.02	4.37 ± 1.14	0.394	0.694
HDL-C (mmol/L)	1.02 ± 0.27	1.08 ± 0.30	1.651	0.099	1.03 ± 0.22	1.08 ± 0.30	1.123	0.263
LDL-C (mmol/L)	2.83 ± 0.86	2.73 ± 0.96	0.991	0.322	2.78 ± 0.82	2.74 ± 0.96	0.260	0.795
CRP (mg/L)	10.76 ± 10.86	19.33 ± 13.59	3.437	< 0.001*	11.34 ± 10.71	19.37 ± 13.68	3.505	< 0.001*
BNP (ng/L)	556.41 ± 1125.30	1180.39 ± 2927.63	2.110	0.035	624.00 ± 882.37	503.12 ± 578.03	0.514	0.608
cTnl (ng/ml)	34.88 ± 64.52	53.55 ± 111.09	2.310	0.021	52.39 ± 92.32	52.63 ± 111.52	0.015	0.988
CK (U/L)	1139.23 ± 1580.77	1455.87 ± 1994.59	1.675	0.094	1226.78 ± 1756.01	1442.91 ± 2004.36	0.710	0.479
LDH (U/L)	440.49 ± 357.39	517.42 ± 534.29	1.763	0.078	452.22 ± 337.43	485.36 ± 456.07	0.511	0.61
K (mmol/L)	4.05 ± 0.45	4.02 ± 0.52	0.590	0.555	4.08 ± 0.39	4.01 ± 0.53	0.895	0.372

Table 4 (continued)

Variables	Before PSM				After PSM			
	Non-MACCE (n = 1086)	MACCE (n = 78)	t/χ2	P-value	Non-MACCE (n = 77)	MACCE (n = 77)	t/χ2	P-value
LVEDD (mm)	49.63 ± 5.72	4.02 ± 0.52	0.590	0.555	49.04 ± 4.71	49.28 ± 7.57	0.216	0.829
LVEF (%)	55.40 ± 12.31	47.62 ± 10.68	3.437	<0.001*	55.72 ± 9.97	47.77 ± 10.68	3.700	<0.001*

PSM Propensity score matching, MACCE Major adverse cardiovascular and cerebrovascular events, CKD Chronic kidney disease, PAD Peripheral arterial disease, PCI Percutaneous coronary intervention, CABG Coronary artery bypass grafting, LM Left main coronary artery, LAD Left anterior descending coronary artery, LCX Left circumflex coronary artery, RCA Right coronary artery, SBP Systolic blood pressure, DBP Diastolic blood pressure, HR Heart rate, RR Respiratory rate, IABP Intra-aortic balloon pump, WBC White blood cell, HGB Hemoglobin, PLT Blood platelet count, ALT Alanine transaminase, ALB Albumin, AST Aspartate aminotransferase, Cr Serum creatinine, Glu First blood glucose on admission within 24 h, HbA1c Glycosylated hemoglobin, SHR Stress hyperglycemia ratio, TG Total triglycerides, TC Total cholesterol, HDL-C High-density lipoprotein cholesterol, LDL-C Low-density lipoprotein cholesterol, CRP C-reactive protein, BNP Brain natriuretic peptide, cTnI Cardiac troponin I, CK Creatine kinase, LDH Lactate dehydrogenase, K serum potassium, LVEDD Left ventricular end-diastolic dimension, LVEF Left ventricular ejection fraction

* P < 0.05

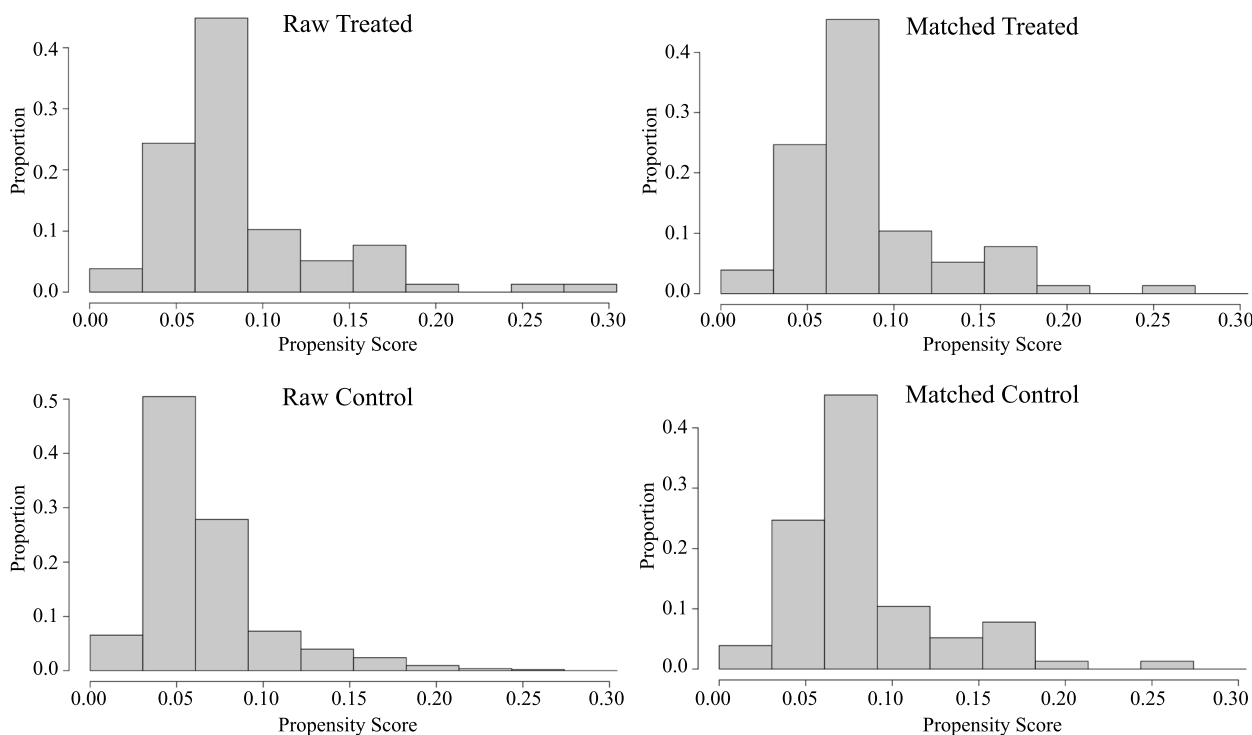


Fig. 4 Clinical features of nondiabetic STEMI patients before and after PSM

Table 5 Multivariate logistic regression analysis of predictors of in-hospital outcomes in STEMI patients without diabetes after PSM

Variables	β	S.E	OR	95%CI	P-value
Arrhythmia	2.82	1.11	16.79	2.72–328.46	0.011*
Killip III&IV	2.66	0.82	14.35	3.47–98.88	0.001*
SHR	2.42	0.73	11.26	3.05–55.21	<0.001*
CRP	0.05	0.18	1.05	1.02–1.09	0.003*

S.E. Standard error, O: Odds ratio, CI Confidence interval, SHR Stress hyperglycemia ratio, CRP C-reactive protein

* P < 0.05

might be masked in diabetic patients because DM itself may lead to poor long-term prognosis. It may also be explained by more severe inflammation in patients with newly diagnosed hyperglycemia than those with known DM [29]. In our subgroup analysis, patients with previously diagnosed DM or significantly elevated HbA1c were excluded, and the effects of stress hyperglycemia on in-hospital outcomes in nondiabetic patients were investigated. The results showed that SHR was also a predictor of MACCE in the nondiabetic subgroup.

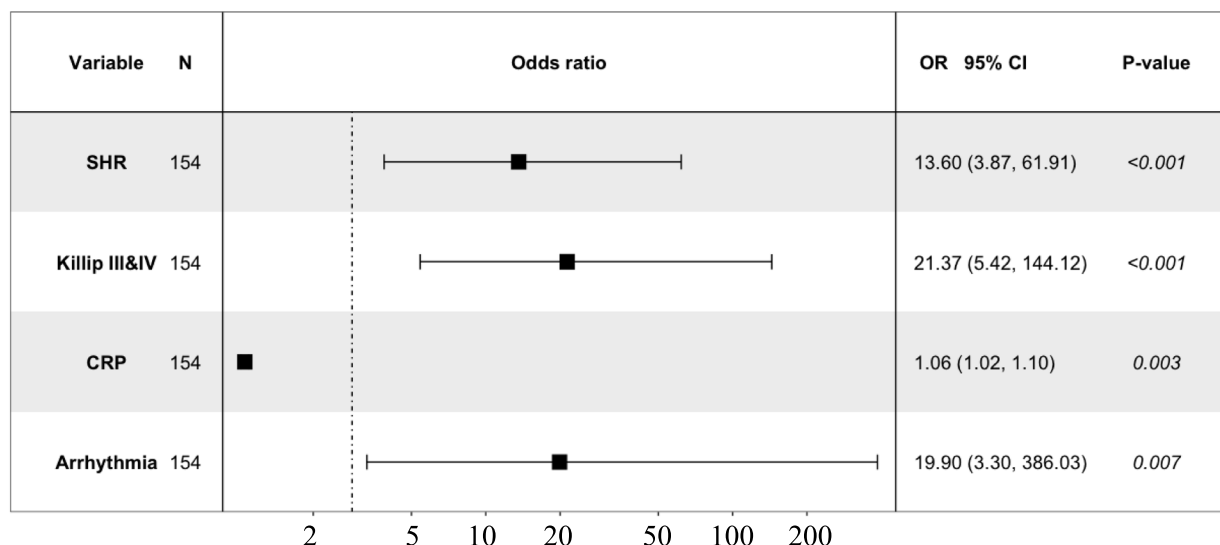


Fig. 5 Multivariate logistic regression analysis of predictors of in-hospital outcomes in the nondiabetic subgroup after PSM

Currently, there is no consensus on the definition and reference interval for stress hyperglycemia. In 2015, Roberts et al. [5] enrolled 2,290 patients admitted to the emergency department and investigated whether critical illness was correlated with relative or absolute hyperglycemia. In their univariate analysis, both the SHR (OR=1.23 mmol/L; 95% CI: 1.18–1.28; $P < 0.001$) and Glu (OR=1.18 mol/L; 95% CI: 1.13–1.23; $P < 0.001$) were independent risk factors for critical illness. In their multivariate analysis, however, only SHR [OR=1.20 95% CI: 1.13–1.28; $P < 0.001$] remained significantly correlated, while Glu [OR=1.03 mmol/L (0.97, 1.11); $P = 0.31$] did not.

The relationship between the SHR and the prognosis of STEMI patients has been previously investigated. In a retrospective study of 4,362 patients with coronary heart disease who underwent PCI in the COACT Registry, the SHR was identified as a predictor for MACCE within 30 days after PCI, especially in nondiabetic patients [6]. A recent prospective, multicenter observational study of 6,287 STEMI patients who were discharged alive showed that a high SHR was significantly correlated with poor long-term prognosis in the nondiabetic population, but not in the diabetic population [29]. Additionally, Chen et al. reported the potential of the SHR as an independent and simple indicator of poor in-hospital prognosis in elderly patients with AMI, especially in the nondiabetic population [30]. The above data are consistent with the results of the present study.

The limitations of this work should also be acknowledged. Firstly, this was a single-center study with a

limited sample size. Secondly, due to the retrospective nature of the study, long-term observation and follow-up after discharge were not performed. Further studies with a prospective design and long-term follow-up are needed. Thirdly, stress may impair the homeostasis of many systems, including the renin–angiotensin–aldosterone system, the sympathetic system, and the inflammatory system, which may ultimately affect in-hospital outcomes.

Conclusion

In conclusion, the SHR, as a new parameter of stress-induced hyperglycemia, is an independent predictor of MACCE in patients with STEMI, especially in the nondiabetic population. The SHR can be easily calculated from HbA1c and Glu, and therefore, can be widely applied in clinical practice for early risk stratification of newly diagnosed STEMI patients.

Abbreviations

SHR	Stress hyperglycemia ratio
MACCE	Major adverse cardiovascular and cerebrovascular events
STEMI	ST-segment elevation myocardial infarction
OR	Odds ratio
DM	Diabetes mellitus
AMI	Acute myocardial infarction
HbA1c	Glycated hemoglobin
PSM	Propensity score matching
cTn	Cardiac troponin
MI	Myocardial infarction
DBP	Diastolic blood pressure
SBP	Systolic blood pressure
HR	Heart rate
IABP	Intra-aortic balloon pump
WBC	White blood cell

CRP	C-reactive protein
Cr	Serum creatinine
BNP	Brain natriuretic peptide
LVEF	Left ventricular ejection fraction
PCI	Percutaneous coronary intervention
CI	Confidence interval
CKD	Chronic kidney disease
PAD	Peripheral arterial disease
CABG	Coronary artery bypass grafting
LM	Left main coronary artery
LAD	Left anterior descending coronary artery
LCX	Left circumflex coronary artery
RCA	Right coronary artery
RR	Respiratory rate
HGB	Hemoglobin
PLT	Blood platelet count
ALT	Alanine transaminase
ALB	Albumin
AST	Aspartate aminotransferase
Glu	Blood glucose
TG	Total triglycerides
TC	Total cholesterol
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
CK	Creatine kinase
LDH	Lactate dehydrogenase
K	Serum potassium
LVEDD	Left ventricular end-diastolic dimension
S.E	Standard error

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Authors' contributions

WG, JJZ and WXL conceived and designed research; WG and JJZ collected data and conducted research, analyzed and interpreted data; WG wrote the initial draft; WXL revised the manuscript; WXL had primary responsibility for final content. All authors read and approved the final version of the manuscript.

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Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available due to limitations of ethical approval involving the patient data and anonymity but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University (Approval number: 2022170X) and was conducted in accordance with the principles of the Declaration of Helsinki. All patients provided written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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